December 19, 2002

Richard Balcomb
Director, Toxicology and Environmental Assessments
Plastic Additives Business Support
Ciba Specialty Chemicals Corporation
540 White Plains Road
Tarrytown NY 10591

Dear Dr. Balcomb:

The Office of Pollution Prevention and Toxics is transmitting EPA's comments on the robust summaries and test plan for 1,6-hexamethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate (CAS No. 35074-77-2) posted on the ChemRTK HPV Challenge Program Web site on August 22, 2002. I commend Ciba Specialty Chemicals Corporation for its commitment to the HPV Challenge Program.

EPA reviews test plans and robust summaries to determine whether the reported data and test plans will provide the data necessary to adequately characterize each SIDS endpoint. On its Challenge Web site, EPA has provided guidance for determining the adequacy of data and preparing test plans used to prioritize chemicals for further work.

EPA will post this letter and the enclosed comments on the HPV Challenge Web site within the next few days. As noted in the comments, we ask that Ciba Specialty Chemicals Corporation advise the Agency, within 60 days of this posting on the Web site, of any modifications to its submission.

If you have any questions about this response, please contact Richard Hefter, Chief of the HPV Chemicals Branch, at 202-564-7649. Submit questions about the HPV Challenge Program through the "Contact Us" link on the HPV Challenge Program Web site pages or through the TSCA Assistance Information Service (TSCA Hotline) at (202) 554-1404. The TSCA Hotline can also be reached by e-mail at tsca-hotline@epa.gov.

I thank you for your submission and look forward to your continued participation in the HPV Challenge Program.

Sincerely,

-S-

Oscar Hernandez, Director
Risk Assessment Division

Enclosure

cc: C. Auer
A. Abramson
W. Penberthy
M. E. Weber

EPA Comments on Chemical RTK HPV Challenge Submission:
1,6-Hexamethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate)

SUMMARY OF EPA COMMENTS

The sponsor, Ciba Specialty Chemicals Corporation, submitted a test plan and robust summaries to EPA on July 29, 2002, for 1,6-hexamethylene bis(3,5-di-tert-butyl-4-hydroxyhydrocinnamate) (CAS No. 35074-77-2). EPA posted the submission on the Chemical RTK HPV Challenge Web site on August 22, 2002.

EPA has reviewed the submission and has reached the following conclusions:

1. Physicochemical Properties and Environmental Fate. Data are adequate for physicochemical properties, photodegradation, biodegradation, and transport and distribution (fugacity). The submitter needs to provide test data for stability in water (hydrolysis) or a technical discussion as to why testing is not necessary for this chemical.

2. Health Effects. Data for acute, repeated-dose, reproductive and developmental toxicity are adequate for the purposes of the HPV Challenge Program. A separate robust summary is needed for the reproductive toxicity endpoint. Data for genetic toxicity are inadequate.

3. Ecological Effects. No testing is recommended for the purposes of the HPV Challenge Program. Toxicity to aquatic organisms is not expected to occur because of the chemical's low water solubility and high log K_{OW}.

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.

EPA COMMENTS ON THE 1,6-HEXAMETHYLENE BIS(3,5-DI-tert-BUTYL-4-HYDROXYHYDROCINNAMATE) CHALLENGE SUBMISSION

Test Plan

Chemistry (melting point, boiling point, vapor pressure, partition coefficient and water solubility).

The data provided by the submitter for these endpoints are adequate for the purposes of the HPV Challenge Program.

Environmental Fate (photodegradation, stability in water, biodegradation, fugacity).

The data provided by the submitter for photodegradation, biodegradation, and transport and distribution (fugacity) are adequate for the purposes of the HPV Challenge Program. Because 1,6-hexamethylene bis (3,5-di-tert-butyl-4-hydroxyhydrocinnamate) contains ester functional groups that may be susceptible to hydrolysis, the submitter needs to test for this endpoint or provide a technical discussion as to why testing is not necessary.

Health Effects (acute toxicity, repeated-dose toxicity, genetic toxicity, and reproductive/developmental toxicity).

Data for acute, repeated-dose, reproductive and developmental toxicity are adequate for the purposes of the HPV Challenge Program. Data for genetic toxicity are inadequate.

Acute toxicity. The submitter needs to correlate the entries in the test plan with the critical studies selected for the robust summaries as described below.

Genotoxicity (gene mutations). The highest dose level tested in the Ames assay was 2000 µg/plate, significantly less than the recommended 5000 µg/plate. The submitter needs to provide information on whether cytotoxicity or the formation of precipitate was a factor relevant to dose selection. In addition, the submitter needs to state whether or not positive, negative and/or solvent controls were used. If such information is unavailable on the selected study, the submitter needs to provide data using the appropriate dose levels.

Genotoxicity (chromosomal aberrations). The submitted dominant lethal assay is not appropriate for addressing chromosomal aberrations in somatic cells. The reported negative results do not address the possibility that (1) the blood/gonad barrier could prevent transfer of chemical to the gonads; and (2) the absence of effects in the gonads does not exclude the possibility of genetic damage in somatic cells. Therefore, the submitter needs to provide information from an in vitro cytogenetics assay using appropriate exposure concentrations in a cultured mammalian cell line (for example, OECD GL 473).

Reproductive Toxicity. An adequate developmental toxicity study and histopathology of the reproductive organs from a 104-week repeated dose toxicity study in rats are acceptable for addressing this endpoint.

Ecological Effects (fish, invertebrate and algal toxicity)

Although the aquatic acute toxicity data submitted for fish, invertebrates and algae were inadequate, EPA recommends no further testing at this time because the uptake of the chemical by aquatic organisms and toxicity to aquatic organisms is unlikely due to the chemical's low water solubility and high calculated log K_{OW} (> 8).

Specific Comments on Robust Summaries

Environmental Fate

Transport and distribution (fugacity). The submitter's treatment of fugacity is adequate, except that the submitter needs to provide the assumption and data inputs to the model (see Guidance for Robust Summary preparation).

Health Effects

Acute toxicity. The submitter needs to correct discrepancies between the test plan and the robust summaries. The test plan refers to 1969 studies for acute oral toxicity (rat LD50 >5000 mg/kg) and acute dermal toxicity (rabbit LD50 >10,000 mg/kg). However, robust summaries are provided for a 1978 Ciba-Geigy, Ltd. oral toxicity study (mice LD50 >7,750 mg/kg) and a 1970 Ciba-Geigy dermal toxicity study (rabbit LD50 > 10,000 mg/kg). The submitter also needs to provide information on the purity of the test substance, and the age and weight of the animals used in the oral toxicity study.

Repeated-Dose Toxicity. The submitter needs to provide information on the purity of the test compound, as well as information on organ weights and histopathology of reproductive organs from the 104-week and other available repeated-dose studies.

Reproductive Toxicity. The submitter needs to provide a separate robust summary for this endpoint based on the submitted developmental and chronic feeding toxicity studies.

Developmental Toxicity. The submitter needs to provide information on the purity of the test compound, if available, and needs to provide the following details: a description of how the fetuses were handled at Caesarean section, namely the number of fetuses per litter examined for external, visceral, or skeletal malformations; the magnitude of reductions in food consumption and body weight gains for dams; and fetal body weight data.

FOLLOWUP ACTIVITY

EPA requests that the submitter advise the Agency within 60 days of any modifications to its submission.